IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:	:	Conf. No.:9053
Mary A. Reppy et al.	:	
Serial No.: 09/811,538	:	Art Unit: 1641
Filed: March 20, 2001	:	Examiner: Tran, My Chaut
For: METHOD FOR DETECTING AN ANALYTE BY FLUORESCENCE	:	Atty Docket: 22001/0005

#13
3-14-03

APPEAL BRIEF

Commissioner for Patents
Washington, D.C. 20231

Sir:

This is an appeal from the Primary Examiner's final rejection of claims 1-19.

I. Real Party in Interest

The real party in interest is the assignee of the application, Analytical Biological Services, Inc.

II. Related Appeals and Interferences

There are no other appeals or interferences known to Appellant, Appellant's legal representative, or assignee which will directly affect or be directly affected by or have a bearing on the Board's Decision in this Appeal.

III. Status of Claims

Claims 1-46 are in the application. Claims 1-19 are finally rejected and are on appeal. Claims 20-46 are directed to non-elected inventions.

IV. Status of Amendments

The amendment to the claims filed after the final rejection has been entered.

V. Summary of Invention

The present invention on appeal relates to detecting an analyte in a sample by contacting the sample to be tested with a three-dimensional array that comprises a polydiacetylene backbone and a substrate wherein the substrate has direct affinity for an analyte or is capable of binding to an analyte or is capable of reacting with an analyte. (See page 5, lines 1-10 of the specification). An analyte, when present, causes a change in fluorescence of the polydiacetylene backbone. (See page 5 lines 11-16). The change in fluorescence is then detected to thereby indicate the presence of the analyte. (Page 5, lines 9-10).

As discussed in the specification measuring the change in fluorescence of the array is a significantly more sensitive test than monitoring by color change.(Page 5, lines 17-19) The increase in sensitivity is crucial for providing detection systems to have actual practical utility as a sensor for many applications where monitoring color change would not be satisfactory. (Page 5, lines 19-20).

Moreover, as discussed in the specification, the assay method of the present invention makes possible a continuous monitoring of the binding or the interaction of an analyte. (Page 5, lines 25-27). Also, since no wash steps are required in the technique of the present invention, the method is relatively simple and inexpensive to carry out. (Page 5, lines 29-30).

VI. Issues

A. Has the Examiner established that claims 1-19 are obvious and therefore unpatentable over the cited art and namely U.S. Patent 5,415,999 to Saul et al in view of U.S. Patent 6,180,135 B1 to Charych et al?

VII. Grouping of Claims

Claim 9 does not stand or fall together with claims 1-8 and 11-19.

VIII. Appellants Arguments

A. U.S. Patent 5,415,999 to Saul et al. in combination with U.S. Patent 6,180,135 B1 to Charych et al. fails to render obvious claims 1-19.

Claims 1-19 were rejected under 35 USC 103 (a) as being unpatentable over U.S. 5,415,999 Saul, et al., in view of US patent 6,180,135 B1 to Charych et al. These cited references do not render obvious the present invention. In particular, the claims under consideration relate to detecting an analyte in a sample by contacting the sample to be tested with a three–dimensional array that comprises a polydiacetylene backbone and a substrate wherein the substrate has direct affinity for an analyte or is capable of binding to an analyte or is capable of reacting with an analyte. An analyte when present causes a change in fluorescence of the polydiacetylene backbone. The change in fluorescence is then detected to thereby indicate the presence of an analyte.

As discussed in the specification measuring the change in fluorescence of the array is a significantly more sensitive test than monitoring by color change. The increase in sensitivity is crucial for providing detection systems to have actual practical utility as a sensor for many applications where monitoring color change would not be satisfactory.

Moreover, as discussed in the specification, the assay method of the present invention makes possible a continuous monitoring of the binding or the interaction of an analyte. Also, since no wash steps are required in the technique of the present invention, the method is relatively simple and inexpensive to carry out.

U.S. patent 5,415,999 to Saul et al, fails to suggest or render obvious the present invention since, among other things, as recognized by the Examiner, Saul et al., fails to suggest or disclose a three-dimensional array of a polydiacetylene backbone or, according to preferred aspects of the present invention, an array that is in the form of the liposomes or tubules (see claims 2, 11 and 13). Furthermore, Saul et al., fails to suggest the present invention since Saul et al is not concerned with a change in fluorescence of a polydiacetylene backbone. Instead, Saul et

al., requires a red, fluorescent, polydiacetylene film that is layered with fluorescence modulation reagent non-covalently associated with the film. This fluorescence-modulating reagent required by Saul et al., modulates the measured emission of the film, e.g., by absorbing the emitted light, in response to the presence of an analyte. In other words, the fluorescent state of the film does not change during the assay; rather, the emission is obscured or revealed by the action of the fluorescence modulation agent required by Saul et al. Saul et al. does not suggest measuring the change in fluorescence that is due to the interaction or binding of an analyte and the polydiacetylene. Nothing whatsoever in Saul et al suggests that the fluorescence of the polydiacetylene would or could be modulated upon analyte binding without the fluorescence modulation layer.

Charych, et al., fails to overcome the above-discussed efficiencies of Saul, et al., with respect to rendering obvious the present invention. In particular Charych, et al., does not relate to using fluorescence but instead relates to a method that monitors color change of a three-dimensional array of a polydiacetylene backbone. Nothing whatsoever in Charych et al., would suggest that the three-dimensional array could be used in a method that detects the change in fluorescence. Furthermore, the three-dimensional arrays suggested by Charych et al., are prepared in the blue form, which is the non-fluorescent form, in order to be suitable for the assays suggested therein. Charych et al suggest a colorimetric change of polydiacetylene liposomes from blue to red in response to the analyte binding or reacting with a substrate incorporated in the liposomes. Since the technique suggested by Saul et al., requires starting with a red fluorescent film it would be counterintuitive to employ the non-fluorescent three-dimensional array suggested by Charych et al., in the method of Saul et al. Accordingly, the prior art lacks any motivation to substitute the polydiacetylene three-dimensional arrays employed by Charych et al., in the method of Saul et al. In fact, if anything, the cited art actually leads from the present invention.

Furthermore, even if such were substituted in the method of Saul et al., the present invention would still not be suggested since, as discussed above, Saul et al., require a fluorescent modulating reagent which obscures or reveals the fluorescence of emissions of the film.

In addition, the Examiner's statement that criticality has not been demonstrating for the use of fluorescence rather than colorimetric polydiacetylene backbone is not germane to this matter, since the Examiner has not even established a *prima facia* case of obviousness. When the proposed modification would change the principle of operation of the prior art being modified, as is the case here, then the teachings of the references are not sufficient to render the claims prima facie obvious. See *In re Ratti* 123 USPQ 349 (CCPA 1959). Furthermore, as discussed in the specification, fluorescence and colorimetric techniques are not the same and fluorescence clearly provides a more sensitive technique. Additionally, the slope of change for the fluorescence measurements is significantly different from that for colorimetric measurements as clearly illustrated in Fig. 3 in this application, which further supports the non-obvious results achieved by the present invention.

Moreover, knowing that the polydiacetylene that Saul et al suggest is fluorescent does not imply that one form of polydiacetylene that Charych suggests would be non-fluorescent while the other form would be fluorescent. There is nothing in either Charych or Saul that would point to **blue** polydiacetylene having different fluorescence characteristics than **red**, or that any change in fluorescence would be of sufficient magnitude for the purpose of detecting analytes. Also, one should keep in mind that conjugated polymers are not necessarily fluorescent. For instance, see McQuade et al. Conjugated Polymer-Based Chemical Sensors, Chem. Rev., 2000, 100, No. 7, pages 2537-2574, June 2000 (copy attached) and particularly page 2538, second complete paragraph.

Additional Reasons as to why Claim 9 Does not Stand or Fall with Claims 1-8 and 10-19.

In addition, Claim 9 which is directed to that aspect of the present invention wherein the polydiacetylene is in the non-fluorescent form is non-obvious since Saul et al., requires a polydiacetylene film that is in the fluorescent form to be suitable for the technique suggested therein. Accordingly, use of a non-fluorescent form would not be suitable for the express purposes of Saul et al.

Discussion of Case Law

The mere fact that cited art may be modified in the manner suggested by the Examiner does not make this modification obvious, unless the cited art suggest the desirability of the modification. No such suggestion appears in the cited art in this matter. The Examiner's attention in kindly directed to *In re Lee* 61 USPQ 2d 1430 (Fed. Cir. 2002) *In re Dembiczak et al.* 50 USPQ2d. 1614 (Fed. Cir. 1999), *In re Gordon*, 221 USPQ 1125 (Fed. Cir. 1984), *In re Laskowski*, 10 USPQ2d. 1397 (Fed. Cir. 1989) and *In re Fritch*, 23, USPQ2d. 1780 (Fed. Cir. 1992).

In Dembiczak et al., supra, the Court at 1617 stated: "Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references. See, e.g., C.R. Bard, Inc., v. M3 Sys., Inc., 157 F.3d. 1340, 1352, 48 USPQ2d. 1225, 1232 (Fed. Cir. 1998) (describing 'teaching or suggestion motivation [to combine]' as in 'essential evidentiary component of an obviousness holding'), In re Rouffet, 149 F.3d 1350, 1359, 47 USPQ2d. 1453, 1459 (Fed. Cir. 1998) ('the Board must identify specifically...the reasons one of ordinary skill in the art would have been motivated to select the references and combine them');...".

Also, the cited art lacks the necessary direction or incentive to those or ordinary skill in the art to render under 35 USC 103 sustainable. The cited art fails to provide the degree of predictability of success of achieving the properties attainable by the present invention needed to sustain a rejection under 35 USC 103. See *Diversitech Corp. v. Century Steps, Inc.* 7 USPQ2d 1315 (Fed. Cir. 1988), *In re Mercier*, 185 USPQ 774 (CCPA 1975) and *In re Naylor*, 152 USPQ 106 (CCPA 1966).

Moreover, the properties of the subject matter and improvements which are inherent in the claimed subject matter and disclosed in the specification are to be considered when evaluating the question of obviousness under 35 USC 103. See *Gillette Co. v. S.C. Johnson & Son, Inc.*, 16 USPQ2d. 1923 (Fed. Cir. 1990), *In re Antonie*, 195, USPQ 6 (CCPA 1977), *In re Estes*, 164 USPQ (CCPA 1970), and *In re Papesch*, 137 USPQ 43 (CCPA 1963).

No property can be ignored in determining patentability and comparing the claimed invention to the cited art. Along these lines, see *In re Papesch*, supra, *In re Burt et al*, 148 USPQ 548 (CCPA 1966), *In re Ward*, 141 USPQ 227 (CCPA 1964), and *In re Cescon*, 177 USPQ 264 (CCPA 1973).

Conclusions

In view of the above, it is abundantly clear that the Primary Examiner erred in finally rejecting claims 1-19. Therefore it is respectfully requested that the Board reverse the Examiner and allow claims 1-19.

In the event that the Examiner deems necessary any further cooperation to further the prosecution of this application, Applicants respectfully urge the Examiner to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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APPENDIX

Claims on Appeal

1. A method for the detection of an analyte in a sample, which comprises contacting the sample to be tested with a three-dimensional array comprising a polydiacetylene backbone and a substrate, wherein the substrate has direct affinity for an analyte or is capable of binding to an analyte or is capable of reacting with an analyte; and wherein a change, if any, in fluorescence of said polydiacetylene backbone is in response to analyte present in said sample;

and detecting the change in fluorescence to indicate the presence of an analyte.

2. The method of claim 1 wherein the array is in the form of a solution of liposomes or tubules.

3. The method of claim 1 wherein the analyte is an enzyme and the substrate is a reactive substrate of that enzyme.

4. The method of claim 1 or 2 wherein the analyte is an antigen and the substrate is the antibody of that antigen.

5. The method of claim 1 or 2 wherein the analyte is an antigen and the substrate is a fragment of the antibody of that antigen.

6. The method of claim 1 or 2 wherein the analyte is an antibody or antibody fragment and the substrate is the antigen of that antibody.

7. The method of claim 1 or 2 wherein the analyte is an antibody or antibody fragment and the substrate is the epitope of that antibody.

8. The method of claim 2 wherein the analyte is an enzyme and the substrate is a reactive substrate of that enzyme.

9. The method of claim 1 wherein the polydiacetylene of the array is in the non-fluorescent form, exhibiting a fluorescent signal that is about 1-3 times that of the background and less than that of the corresponding fluorescent form.

10. The method of claim 1 wherein the substrate includes a ligand.

11. The method of claim 10 wherein the array is in the form of a solution of a liposome or tubule.

12. The method of claim 1 wherein the substrate includes a reactive substrate.

13. The method of claim 12 wherein the array is in the form of a solution of a liposome or tubule.

14. The method of any one of claims 1 to 13 wherein the three-dimensional array further comprises a fluorophore and wherein the change in fluorescence of the polydiacetylene array is monitored.

15. The method of any one of claims 1 to 13 wherein the three-dimensional array further comprises a fluorophore and wherein the change in fluorescence of the fluorophore is monitored.

16. The method of claim 1 wherein the array does not contain a further fluorophore.

17. The method of claim 1 wherein the change in fluorescence is detected by exposure to light having wavelengths below 550 nm and measurement of the emission.

18. The method of claim 1 wherein the change in fluorescence is detected by exposure to light having wavelengths between 450 and 500 nm and measurement of the emission.

19. The method of claim 1 wherein the polydiacetylene of the array exhibits fluorescence and the fluorescence increases as an indication of the presence of the analyte.